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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Rec'd PCT/PTO 28 FEB 2005

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
10104SG63/HFA/PDR		
International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/SG2003/000205	29 August 2003	29 August 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl.[7] C12N 15/62, A61K 39/35

Applicant

NATIONAL UNIVERSTIY OF SINGAPORE et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 11 sheet(s).

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [X] Certain observations on the international application

Date of submission of the demand	Date of completion of the report
25 March 2004	16 December 2004
Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**Gillian Allen** Telephone No. (02) 6283 2266

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/SG2003/000205

I. Basis of the report

1. With regard to the **elements** of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages **2-5, 8, 10, 11, 13, 14, 16-25, 27-29, 33, 35-45** as originally filed,
  pages **1, 6, 9, 12, 15, 26, 30-32, 34** filed with the demand,
  pages , received on with the letter of
- [X] the claims, pages **46-49** as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages , received on with the letter of
- [X] the drawings, pages **1/11-11/11** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [X] the sequence listing part of the description:
  pages **1-13** , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/SG2003/000205

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-32	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-32	NO
Industrial applicability (IA)	Claims	1-32	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Citations

D1 Toda Masako et al. DNA vaccine using invariant chain gene for delivery of CD4+ T cell epitope peptide derived from Japanese cedar pollen allergen inhibits allergen-specific IgE response. Eur J Immunol, 2002. 32(6): 1631-1639.

D2 Wu Tzyy-Chouu et al. Engineering an intracellular pathway for major histocompatibility complex class II presentation of antigens. Proc Natl Acad Sci USA, 1995. 92(25): 11671-75.

D3 WO 2000/50044 A (TAI JUNE YOO) 31 August 2000)

Novelty

The prior art does not disclose the DNA vaccines and constructs of the present claims. Therefore all claims are accepted as novel.

Inventive Step

The invention is directed to DNA vaccines that produce a protective immune response against allergens. The applicants have used known signal sequences fused to the allergen as a construct that achieves this result. The signal sequences target the endoplasmic reticulum/endosome/lysosome to direct antigen presentation to the MHC Class II pathway, which induces Th 1 type immunity, and suppresses the IgE mediated allergic response.

The closest prior art is represented by D1 and D2.

D1 discloses that allergic responses to an allergen can be inhibited using a DNA construct that targets the allergen to the MHC II antigen presentation pathway. This induces a Th 1 response. The Th 1 immune response results in inhibition of the IgE mediated allergic response. The targeting sequence is an MHC II invariant chain Ii, that includes a signal sequence targeting the endosome/lysosome compartments. The citation teaches use of the construct as a DNA vaccine, and booster immunisation with the allergenic protein. The citation differs from the present application in that the present application uses different constructs to target the allergen to the MHC II pathway.

D2 discloses that antigenic peptides can be directed into the MHC II/Th 1 pathway using LAMP-1 signal sequences to route the antigen into the endosomal and lysosomal compartments. D2 discloses constructs that comprise the LAMP-1 N terminal signal sequence linked to an immunogen, linked to the LAMP-1 transmembrane sequence and cytoplasmic tail. The N terminal signal sequence is stated in the present specification to locate the protein to the endoplasmic reticulum. The LAMP-1 transmembrane domain and cytoplasmic tail are stated in the present specification to comprise a signal sequence that locates the protein to the endosome or lysosome, see description pp 30 32. The constructs of D2 are identical to constructs

Continued in Supplemental Box V

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

NOTE:

Claims 16-32 are to methods of treatment of humans and animals. The applicants are warned that, should this application proceed to National Phase, such claims may not be acceptable in all jurisdictions under the PCT.

Supplemental Box V
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Inventive Step

encompassed by claims 1-14, except that the protein of the citation is an antigen, and that of the present application an allergen.

It would be obvious to one skilled in the art that D2 discloses alternate constructs to those disclosed in D1 for directing peptides into the MHC II antigen presenting pathway. Thus the construct comprising LAMP-1 N-terminal signal sequence and C-terminal transmembrane and cytoplasmic domains provides an obvious alternate structure to that of D1 for redirecting the antigen to the MHC II pathway, and the claimed constructs cannot be accepted as inventive over D1 in light of D2.

The use of constructs that direct the allergen into the MHC II pathway as vaccines protecting against IgE mediated allergic effects, and vaccination methods including booster immunisation with the allergenic protein are disclosed in D1. Thus the use of the claimed constructs as vaccines is not inventive over D1 in light of D2.

The pathway leading to MHC class II antigen presentation is well known. One skilled in the art would be aware that other proteins having cellular locations similar to that of LAMP-1 would have N- and C-terminal sequences useful in the present invention. In the absence of any indication that the signal peptides other than LAMP-1, encompassed by claims 3 and 6, provide constructs that have unexpected properties differing from those of LAMP-1, the choice of alternate signal peptides does not provide invention.

The choice of allergen from among known allergenic proteins or peptides does not confer invention, as the choice of allergenic peptide has no influence on the antigen presentation pathway.

The methods of administration and time required to induce long term immune memory are parameters that could readily be determined by one skilled in the art.

Therefore none of the claims is considered inventive over D1 in light of D2.

The applicants have submitted arguments against inventive step, but these arguments were not deemed to be relevant to the invention as defined by the present claims.